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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/730,379	12/09/2003	Barton F. Haynes	1579-871	2849

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EXAMINER	
KIM, YUNSOO	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 06/20/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/730,379	HAYNES, BARTON F.	
	Examiner	Art Unit	
	Yunsoo Kim	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 March 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-9 are pending.

2. In view of Applicants amendment to the claims, the rejection under 35 U.S.C. 112, second paragraph (sections 4-5) in the office action mailed 9/29/05 has been withdrawn.

3. In further consideration of the instant application, the new ground rejections have set forth herein.

4. The use of trademarks has been noted in this application (e.g. Tween-20®, FACSLYSE®, FACStar Plus® on p. 13). Each letter of the trademarks should be capitalized wherever it appears and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent application, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1-9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(a) Claims 1-9 are indefinite in the recitation of K12 because its characteristics are not known. The use of K12 as the sole means of identifying the claimed polypeptide renders the claims indefinite because K12 is merely a laboratory designation which does not clearly define the claimed product, since different laboratories may use the same laboratory designations to define completely distinct polypeptides. In addition, the specification of the instant application, p. 6, defines K12 to include any protein described in the US Pat. 6,350,615. The '615 patent only discloses one species of K12, SEQ ID NO:1 It is not clear as to what other protein structures are qualified as K12.

Applicant is invited to identify the polypeptides by the SEQ ID NO:1 of the '615 patent.

(b) Claims 7-9 have no antecedent basis in base claim 1. Claims 7-9 are drawn to a method of enhancing immune response by administering a nucleic acid to encode the polypeptide, wherein base claim 1 is drawn to a method of enhancing immune response by administering a polypeptide.

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1-9 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of enhancing an immune response with a polypeptide consisting of the extracellular domain of K12 as identified by SEQ ID NO:1 of the U.S. Patent 6,350,615, does not reasonably provide enablement for any method of enhancing an immune response comprising "portion" of any K12, 95% homologous to extracellular domain of any K12 and **any peptide " comprising" the extracellular domain of any K12 as recited** in claim 1.

Applicants' argument filed 3/29/06 has been fully considered but was not persuasive.
Applicants argue that the claims as amended do not recite " mimetics thereof" and the specification is fully enabled.

The examiner's position is that the specification provides guidance of an polypeptide consisting of the extracellular domain of K12 defined by SEQ ID NO:1 of the '615 patent. The specification fails to provide any guidance as to the structures of other K12 proteins.

Further, the "portion" reads on any fragment of extracellular domain of any K12, and "95% homologous" to extracellular domain of any K12 encompasses the vaccine composition comprising any deletion, substitution or addition of undisclosed amino acids. As stated in the previous office action, minor structural differences among structurally related compounds or compositions can result in substantially different or deleterious biological activities.

In addition, the claimed method includes enhancing an immune response by any polypeptide **comprising** the extracellular domain of any K12. The term "comprising" is open-ended. It expands the amino acid

sequence of the polypeptide to include additional non-disclosed amino acids. The specification does not provide sufficient guidance as to which amino acid sequence within the polypeptide can be unique and retain a distinct functional capability of the extracellular domain of any K12.

Ngo *et al* teach that the amino acid positions within the polypeptide/protein that can tolerate change such as conservative substitution or no substitution, addition or deletion which are critical to maintain the protein's structure will require guidance (see Ngo et al., 1994, The Protein Folding Problem and Tertiary Structure Prediction, pp. 492-495 in particular, of record).

The art acknowledges that function cannot be predicted based solely on structural similarity to a protein found in the sequence databases and recognized that it was unpredictable if any functional activity will be shared by two polypeptides having less than 100% identity over the full length of their sequences. Attwood (Science 2000; 290:471-473) teaches that "[i]t is presumptuous to make functional assignments merely on the basis of some degree of similarity between sequences. Similarly, Skolnick et al. (Trends in Biotech. 2000; 18(1):34-39) teach that the skilled artisan is well aware that assigning functional activities for any particular protein or protein family based upon sequence homology is inaccurate, in part because of the multifunctional nature of proteins (e.g., "Abstract" and "Sequence-based approaches to function prediction", page 34). Even in situations where there is some confidence of a similar overall structure between two proteins, only experimental research can confirm the artisan's best guess as to the function of the structurally related protein (see in particular "Abstract" and Box 2). Finally, even single amino acid differences can result in drastically altered functions between two proteins. For example, Metzler et al. (Nature Structural Biol. 1997; 4:527-531) show that any of a variety of single amino acid changes can alter or abolish the ability of CTLA4 to interact with its ligands CD80 and CD86 (e.g., summarized in Table 2). Thus it is unpredictable if any functional activity will be shared by two polypeptides having less than 100% identity over the full length of their sequences.

In re Fisher, 166 USPQ 18 indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. Since the amino acid sequence of a polypeptide determines its structural property, predictability of which amino acid fragment can retain the functional capabilities of the "portion of any K12,", 95% homologous to extracellular domain of any K12, comprising polypeptide and any polypeptide comprising the extracellular domain of any K12 requires knowledge of, and guidance with regard to, which segments in the polypeptide's sequence contribute to its function. The

specification only provides guidance of a polypeptide consisting of an extracellular domain of K12 defined by the SEQ ID NO:1 of the '615 patent.

Therefore, there is insufficient direction as to how to make and to use a vaccine composition comprising any "portion of any K12", 95% homologous to extracellular domain of any K12 and any polypeptide comprising the extracellular domain of any K12 which can be used as to whether such a desired effect can be achieved or predicted, as encompassed by the claims.

In view of the quantity of experimentation necessary, the limited working example, the unpredictability of the art, the lack of sufficient guidance in the specification, and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

Moreover, the incorporation of essential material in the specification by reference to an unpublished U.S. application, foreign application or patent, or to a publication is improper. Applicant is required to amend the disclosure to include the material incorporated by reference, if the material is relied upon to overcome any objection, rejection, or other requirement imposed by the Office. The amendment must be accompanied by a statement executed by the applicant, or a practitioner representing the applicant, stating that the material being inserted is the material previously incorporated by reference and that the amendment contains no new matter. 37 CFR 1.57(f).

The attempt to incorporate subject matter into this application by reference to US 20020141999 on page 6, lines 22-25 of the specification of the instant application is ineffective because the essential material in the specification can only be incorporated by the issued US patents (e.g. U.S. Pat. 6,350,615).

9. Claims 1-9 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is in possession of a vaccine composition comprising of the polypeptide consisting of extracellular domain of K12 as identified by the SEQ ID NO:1 of the U.S. Pat. 6,350,615; however, applicant is not in possession of a vaccine composition comprising "portion of any K12", 95%

homologous to extracellular domain of any K12 and **any polypeptide comprising the extracellular domaion of any K12.**

Applicants' argument filed 3/29/06 has been fully considered but was not persuasive.
Applicants argue that the claims as amended do not recite " mimetics thereof" and the specification is fully enabled.

The examiner's position is that there is insufficient written description encompassing "portion of any K12","95% homologous" to extracellular domain of any K12and any polypeptide comprising the extracellular domain of any K12 because any chemical or physical properties (i.e. chemical structure or specific amino acid changes lead to said function) of "portion of any K12," , 95% homologous to extracellular domain of K12 and any polypeptide comprising the extracellular domain of any K12 are not set forth in the specification as filed, commensurate in scope with the claimed invention.

Claims 1-9 read on any portion of any K12 (or fragment), 95% homologous to extracellular domain of any K12 , and any polypeptide comprising the extracellular domain of K12 include any polypeptide that has a portion of any K12 or 95% homologous to extracellular domaion of any K12 or extracellular domain of any K12 and the genus encompasses the limitations is extremely large.

In addition, the claimed method includes enhancing an immune response by any polypeptide **comprising** the extracellular domain of K12. The term "comprising" in claim 1 is open-ended. It expands the amino acid sequence of the polypeptide to include additional non-disclosed amino acids. The specification p. 6-7 of the instant application does not describe any representative of genus encompassed by the limitations.

Therefore, Applicant does not possess of scope of claimed invention. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of use.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to

recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

> e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

11. Claims 1-6 are rejected under 35 U.S.C. 102 (e) as being anticipated by U.S. Pat. No. 6,762,030 B2 (of record) as is evidenced by the specification of instant application p. 6 (line 8-28) and Singh et al. (Nature Biotechnology, vol. 17, p. 1075-1081), newly cited.

The '030 patent teaches a method of administering soluble human K12 to mammal to induce interferon gamma production, NK cell proliferation (i.e. enhancing immune response, col. 9, lines 36-59, in particular), K12 fusion proteins (i.e. K12-poly-His Flag, K12/hu IgG, Fig 2, col. 3-4 overlapping paragraph, in particular) and the therapeutic uses can be extended to human (col. 17, lines 41-6, in particular). The '030 patent also teaches the soluble human K12 (col. 6, lines 4-7).

As the specification of the instant application (p. 6, lines 26-28) discloses the soluble K12 lacks the functional trans-membrane domain and includes the entire extracellular domain of human K12 thus the referenced soluble K12 would bind to CD7.

The '030 patent further teaches the soluble K12 may include the homologous analogs (col. 6, lines 26-46, in particular) and a nucleic acid that encodes a protein including vector (col. 10, lines 41-45, in particular).

Applicants' arguments filed 3/29/06 have been fully considered but they are not persuasive. Applicants traversed the rejection based on that the claimed limitation is not taught in the cited reference.

The instant specification p. 6 defines the present invention as an " adjuvant" and as is further evidenced by Singh et al., p. 1075, col. 1, 2nd paragraph, the immunological adjuvants were defined as "any substances used in combination with a specific antigen that produce more immunity than the antigen alone" and the soluble K12 enhances interferon gamma production and NK cell proliferation (e.g. enhancing immune response) and "enhancing a vaccine-induced" immune response as recited in claim 1 is an inherent property of an adjuvant.

By the definition, any adjuvant would enhance more immune response than antigen (e.g vaccine), the referenced soluble K12 enhances interferon gamma proliferation and NK cell proliferation (e.g. enhancing immune response) and "enhancing a vaccine-induced" immune response as recited in claim 1 is an inherent property of an adjuvant. Thus, prior art teachings anticipate the instant claimed invention.

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. Claims 1 and 7-9 are rejected under 35. U.S.C. 103(a) as being unpatentable over U.S. Pat. No. 6,762,030 B2 (of record) as is evidenced by the specification of instant application p. 6, lines 8-28 and Singh et al. (Nature Biotechnology, vol. 17, p. 1075-1081) in view of Kwang (Nature Biotechnology, vol. 18, p. 1145-1146).

The teachings of the '030 and Singh et al. have been discussed, supra.

Claim 9 is included because the reference teaches "vector" and the nucleic acid encodes protein and any nucleic acid vector intends to produce protein has an operable promoter.

The '030 patent does not teach a method of enhancing an immune response by administering a nucleic acid encoding the protein.

However, Kwang teaches the major advantages of DNA vaccines (e.g. delivering a gene in a mammal to encode a protein of interest and elicit immune response) over the conventional vaccines are more effective and safe (p. 1145, col. 1).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made administering a nucleic acid encoding a desired protein as taught by Kwang wherein the desired protein is taught by the '030 patent.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because the administering a nucleic acid encoding a protein of interest as taught by Kwang yields safer and more effective vaccine.

From the teachings of the references, one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of the ordinary in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

14. Claims 1-6 are rejected under 35. U.S.C. 103(a) as being unpatentable over U.S. Pat. No. 6,762,030 B2 (of record) as is evidenced by the specification of instant application p. 6, lines 8-28 in view of Singh et al. (Nature Biotechnology, vol. 17, p. 1075-1081).

The reference teachings have been discussed, supra.

The '030 patent does not teach a method of "enhancing a vaccine- induced" immune response by administering to a mammal receiving said vaccine an amount of a polypeptide that comprises the extracellular domain of K12.

However, Singh et al. teaches that the immunological adjuvants were defined as " any substances used in combination with a specific antigen that produces more immunity than the antigen alone" (p. 1075, col. 1, 2nd paragraph).

As is evidenced by the instant specification on p. 6, lines 8-28, which discloses that the adjuvants would enhance more immune response than antigen (e.g. vaccine) and enhance interferon gamma and NK cell production. The soluble extracellular domain of K12 taught by the '030 patent enhances interferon gamma production and NK cell proliferation. Thus, the referenced soluble extracellular domain of K12 works as an adjuvant.

Therefore, it would have been obvious to one of the ordinary skill in the art at the time the invention was made use the soluble extracellular domain of K12 composition taught by the '030 patent in a method of enhancing a vaccine induced immune response.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because the method of enhancing an immune response by administering of the soluble extracellular domain of K12 stimulates interferon gamma production and NK cell production as taught by the '030 patent. As is evidenced by the instant specification on p. 6, lines 8-28, the extracellular domain of K12, as an adjuvant, enhances the production of interferon gamma and NK cells. Also, Singh et al. teaches on p. 1075, col. 1, 2nd paragraph, that the immunological adjuvants were defined as "any substances used in combination with a specific antigen that produce more immunity than the antigen alone". As the claimed soluble extracellular domain of K12 has the same adjuvant effect as the soluble extracellular domain of K12 of the'030 patent, it is expected the soluble extracellular domain of K12 as taught by the '030 patent would elicit the vaccine- induced immune response when it is used in a method of enhancing a vaccine-induced immune response comprising administering to a mammal receiving said vaccine an amount of a polypeptide that comprises the extracellular domain of K12.

From the teachings of the references, one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of the ordinary in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

15. Claims 1 and 7-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over 6,762,030 B2 (of record) as is evidenced by the specification of instant application p. 6 (line 8-28) in view of Singh et al. (Nature Biotechnology, vol. 17, p. 1075-1081) as applied to claims 1-6 above, and further in view of Kwang (Nature Biotechnology, vol. 18, p. 1145-1146).

The teachings of the '030 and Singh et al. have been discussed, supra.

Claim 9 is included because the reference teaches "vector" and the nucleic acid encodes protein and any nucleic acid vector intends to produce protein has an operable promoter.

The '030 patent does not teach a method of enhancing an immune response by administering a nucleic acid encoding the protein.

However, Kwang teaches the major advantages of DNA vaccines (e.g. delivering a gene in a mammal to encode a protein of interest and elicit immune response) over the conventional vaccines are more effective and safe (p. 1145, col. 1).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made administering a nucleic acid encoding a desired protein as taught by Kwang wherein the desired protein is taught by the '030 patent.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because the administering a nucleic acid encoding a protein of interest as taught by Kwang et al. yields safer and more effective vaccine.

From the teachings of the references, one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of the ordinary in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

16. No claims are allowable.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yunsoo Kim whose telephone number is 571-272-3176. The examiner can normally be reached on Monday thru Friday 8:30 - 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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